REMARKS

Status of the Claims and Claim Amendments

By way of this response, claims 8, 30 and 31 are amended. Support for the amendments to the claims can be found throughout the specification and claims as originally filed (herein referred to as "the Specification"). The amendments discussed herein do not constitute an admission regarding the patentability of the amended subject matter and should not be so construed. Applicant reserves the right to pursue the cancelled or withdrawn subject matter in this or any other appropriate patent application.

The Applicant takes this opportunity to thank the Office for withdrawal of the objection to claims 30 and 31 made in the previous office action. The Applicant also appreciates the withdrawal of the rejections to claim 8, 27 -29 and 33-35 under 35 U.S.C. § 112 (previously rejected on enablement and written description grounds).

As of the recent office action dated December 3, 2008, claims 1, 8, 14-16, and 18-35 are pending in the instant application. Claims 14-16 and 18 -22 were previously withdrawn from consideration. Upon entry of the amendment, Applicant submits that claims 1, 8, and 23- 35 are in condition for allowance.

I. Objection to Claim 8

Claim 8 was objected to because the claim allegedly lacked internal antecedent basis. As requested by the office, the word "one" has been introduced after "said" in line 8 of claim 8. Withdrawal of the objection as moot is respectfully requested.

II. Rejection under 35 U.S.C. § 112, First Paragraph –Enablement

The Office rejected claims 8 and 27-35 on the basis that the specification, "while being enabling for a method of screening or testing for candidate anti-fungal compounds that impair *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1)...by determining whether the candidate compound is a CCA1 inhibitor in a tRNA nucleotidyl transferase assay" the specification allegedly lacks enablement with respect to "determining whether the candidate compound is a CCA1 inhibitor in a growth inhibition assay or binding assay or translation inhibition assay." Office Action, page 8. In the interest of obtaining swift issuance of a patent, and without providing any admission or disclaimer, Applicant respectfully submits that the rejection has been rendered moot in light of the amendments made to claim 8. The Applicant respectfully requests that the rejection be withdrawn.

III. Rejections under 103(a)

The Office rejected independent claim 1 (and claims dependent from claim 1 including 23-26) and independent claim 8 (and claims dependent from claim 8 including 27-35) as allegedly being unpatentable over Weinstock et al. (herein referred to as "Weinstock") in view of one or more additional references. Specifically, the Office asserted that:

> Weinstock et al. discloses nucleic acid sequence[s] relating to *C. albicans*. Table 2, discloses the CCA1 of *C. albicans* contig 3807; column 10 of table 2 provides the name of the organism that was identified as having the closest homology match in this case *S. cerevisiae* and column 11 of the table provides the product name and the function....Thus Weinstock et al. discloses *C. albicans* CCA1.....

Office Action, page 4; *see also* Office Action, p. 11.

Claim 1 is directed to a method of screening or testing for candidate anti-fungal compounds that impair *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) activity comprising: a) providing fungal *Candida albicans* CCA1; b) providing one or more candidate compounds; c) contacting said CCA1 with said one or more candidate compounds; and d) determining the ability of the candidate compound to inhibit CCA1 activity.

Claim 8, as amended, is directed to a method of screening or testing for candidate anti-fungal compounds that impair *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) activity-comprising: a) providing a C. *albicans* cell wherein the cell expresses *Candida albicans* ATP(CTP):tRNA nucleotidyltransferase enzyme (CCA1) under the control of a heterologous promoter; b) providing one or more candidate compounds; c) contacting said one *Candida albicans* cell(s) with the said candidate compounds; d) determining whether the candidate compound inhibits growth or viability of the cell(s); and e) determining whether the candidate compound is a CCA1 inhibitor in a tRNA nucleotidyl transferase assay.

Applicant respectfully disagrees with the assertion by the Office that Weinstock in view of the other references cited by the Office discloses *C. albicans* CCA1 in a manner that renders the subject matter of claims 1 and 8 obvious.

A. The Office Has Not Established a Prima Facie Case of Obviousness.

The Examiner bears the burden of factually supporting any prima facie conclusion of obviousness. M.P.E.P. § 2142. In order to establish a prima facie case of obviousness, the prior art must suggest modifications to arrive at the claimed subject matter. *Takeda Chem. Indus., Ltd.*

v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356 (Fed. Cir. 2007) (a post-*KSR* Federal Circuit decision finding a claimed chemical species not invalid for obviousness). The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. MPEP § 2144.08; *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

For example, in *In re Baird*, a generic diphenol formula was disclosed in a prior art reference cited by the examiner. The reference contained a large number of variables only one of which was the Applicant's claimed species, i.e. bisphenol A. The Federal Circuit found that the prior art reference "unquestionably" encompassed bisphenol A. However, the Federal Circuit found that upon consideration of the reference *as a whole and for all that it teaches*, the reference appeared to teach away from the selection of bisphenol A in favor of more complex species because none of the examples or preferred embodiments were directed specifically to bisphenol A, nor did the disclosure provide any particular guidance preferring bisphenol A over any other species. *In re Baird*, 51 F.3d at 1552 – 1558.

As in *In re Baird*, in this case the Weinstock reference cited by the Office purports to predict an extremely large genus of nucleic acids, and to the extent Weinstock discloses CCA1 of *C. albicans*, it is certainly not preferred. The Weinstock reference discloses over 50,000 nucleic acid sequences encompassing over 800 pages of a single patent reference where the Office has alleged that only one nucleic acid sequence, i.e. contig. 3807, in view of additional references, renders the subject matter of instant claims 1 and 8 obvious.

Applicants submit that when the Weinstock reference is viewed for all that it teaches, Weinstock teaches away from claims 1 and 8 reciting CCA1 of *C. albicans*. Weinstock predicts several nucleic acid sequences of *C. albicans* other than CCA1. For example, Weinstock discloses contig. 5565 at columns 51 and 52 which purports to disclose a nucleic acid that is predicted to code for an actin protein with *C. albicans* as the organism identified as having the closest homology. Thus, to the extent the voluminous Table 2 of Weinstock provides any teaching with respect to *C. albicans*, it teaches, *e.g.*, a prediction of a nucleic acid coding for actin and other proteins identifying *C. albicans* as the organism with the closest homology, but not the nucleic acid encoding CCA1.

The Office points to contig. 3807 from Weinstock's Table 2 (predicting CCA1 of *S. cerevesiae*) asserting that it discloses CCA1 of *C. albicans*. Office Action, p. 4. However, the

Weinstock reference discloses that "Table 2...provides a list of open reading frames (ORFs) in both strands and a *putative* identification of the particular function of a polypeptide...based on the homology match...of the *predicted* polypeptide." Col. 20, lines 52 – 58 (emphasis added). When Weinstock is viewed as a whole, for all that it teaches, contig 3807 is disclosed as CCA1 with the closest homology to *S. cerevisiae*, and not *C. albicans*. Thus, CCA1 is just one of over 50,000 nucleic acid sequences that, at best, is only putatively (or potentially) homologous to *C. albicans*, but has the closest homology to *S. cerevisiae*.

Moreover, the Applicant submits that prior to the filing date of the instant application, it was not known that CCA1 was an essential protein in *C. albicans*. If it was known prior to the inventive date of the instant application that CCA1 was a target in *C. albicans* as a matter of fact, such evidence would be available in the prior art. For example, Weinstock, which discloses over 50,000 other nucleic acid sequences, would have certainly disclosed the organism with the closest homology to the CCA1 nucleic acid as *C. albicans* (as it did with respect to contig 5565 (predicting actin protein) and numerous other nucleic acid sequences predicting *C. albicans* proteins other than CCA1). Rather, only through the use of imperssible hindsight has the Office selected the contig. 3807 sequence from the Weinstock reference in view of additional references to allegedly render the subject matter of claims 1 and 8 obvious. In direct violation of M.P.E.P. § 2145 (X.A.), the § 103(a) rejections made by the Office rely on "knowledge gleaned from applicant's disclosure," which, at a minimum, is the knowledge that CCA1 is an essential protein in *C. albicans*. *See, e.g.,* Specification, Examples 4 and 5.

B. This is Not a Case of "Obvious to Try" or a Combination of References With an Expectation of Success.

Neither the "obvious to try" rationale nor any other obviousness rationale based on a "reasonable expectation of success" is applicable in this case. In order for the Office to reject a claim on the basis of the "obvious to try" rationale, the Office must establish, *inter alia*, "a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem" and a "a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success." M.P.E.P. § 2143. In this case there is neither a finite number of solutions of *C. albicans* targets nor a reasonable expectation of success based on the Weinstock reference in view of the additional references cited by the Office.

The leading case of a "finite number of predictable potential solutions" as set forth in the M.P.E.P. is *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007). In that case, the court rejected the notion that unpredictability could be equated with nonobviousness of a particular salt form of a known active ingredient because there were only a finite number (53) of pharmaceutically acceptable salts to be tested for improved properties. However, as discussed herein, in this case, the Weinstock reference discloses over 50,000 nucleic acid sequences as potential target sequences for *C. albicans*, which can hardly be said to represent a finite and predictable number.

The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. M.P.E.P. § 2143.02; *see also Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08, 18 USPQ2d 1016, 1022-23 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991) (In the context of a biotechnology case, the Federal Circuit refused to find the claimed subject matter obvious because the references did not show that there was a reasonable expectation of success.). In the instant case, it is known that not all proteins essential in *S. cerevisiae* are also essential in *C. albicans*. *See,* Specification, p. 2, lines 3 -5. Moreover, as further discussed in response to the previous Office Action and in the Specification, even for relatively closely related organisms such as *S. cerevesiae* and *C. albicans*, there are significant differences between the two species that make such *in silico* predictions of the type made in Weinstock unreliable. *See, e.g.*, Specification, p. 2, lines 1-3. Therefore, any assertion by the Office that a person of ordinary skill in the art could have pursued any number of potential solutions with a reasonable expectation of success is contrary to the state of the art as of the filing date of the instant application, as disclosed in the Applicant's Specification.

C. The Additional References Cited Do Not Cure The Deficiencies of The Weinstock Reference.

For at least the reasons made of record in responses to the previous Office Actions and for at least the reasons discussed herein, Applicant submits that no combination of the references cited by the Office can render the subject matter of claims 1 and 8, and claims dependent thereon, obvious. *See, e.g.,* response of August 28, 2008 to non-final Office Action, pp. 10-17. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. M.P.E.P. § 2143.01. Applicants submit that neither Onishi et al., Chen et al.,

Georgopapadakou, Nakayama et al., nor any other reference, or combination of references, cited by the Office will cure the deficiencies of Weinstock as discussed herein. Because Weinstock is a primary reference upon which the Office has relied for each of the rejections under § 103(a), for at least the reasons discussed herein, Applicant respectfully requests that any outstanding rejections be withdrawn, and respectfully request that the Office issue a notice of allowance in this case.

CONCLUSION

For at least the foregoing reasons, it is respectfully submitted that claims 1, 8, and 23- 35 are in condition for allowance. Early and favorable consideration is respectfully requested, and the Examiner is encouraged to contact the undersigned at (858) 350-2300 with any questions or to otherwise expedite prosecution.

Respectfully submitted,
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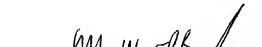

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